REMARKS

Applicants have reviewed the Office Action mailed on September 19, 2005 and offer the following remarks. Claims 17-30 are under consideration. Amendments to the Specification address objections made by the Examiner. No new matter has been added.

Objections to the Specification

The Examiner has objected to the disclosure as it contains an embedded hyperlink. Applicants have removed all hyperlinks from the specification.

The Examiner has indicated that the listing of references in the specification is not a proper information disclosure statement and that they have not been considered.

Applicants do not believe there is a listing of references in the specification and request that the Examiner identify where this listing of references is located.

Claim Rejections

35 U.S.C. § 101

Claims 17 to 30 were rejected under 35 U.S.C. § 101 as being drawn to an invention with no apparent or disclosed specific and substantial credible utility. The Examiner argues that the putative transporter protein of the instant invention and antibodies that bind specifically thereto lack a specific and substantial utility because the instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process which one would wish to diagnose, measure or manipulate for a desired clinical effect. The instant polypeptide is identified as an orphan transporter where the identity of the physiological processes moderated by it are not known. Absent this, antibodies against the protein have neither a specific or substantial utility. The

instant specification does not disclose a credible, specific and substantial "real world" use for applicant's protein and the protein is of undetermined functional and biological significance. Until some actual and specific significance can be attributed to the putative transporter protein of the instant invention, the Examiner concludes the claimed invention is incomplete and does not meet the requirements of 35 U.S.C. § 101 as being useful.

35 U.S.C. § 112

Claims 17 to 30 were rejected under 35 U.S.C. § 112, 1st paragraph, for failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

Applicants respectfully disagree. Applicants have identified the instant protein of SEQ ID NO: 2 as an anion transporter. As stated in the specification on page 5, this protein belongs to the SLC26 family and has been identified as being a transporter of chloride, oxalate and sulfate. Expression of this protein is found in the head/neck and fetal lung (Specification, page 14, lines 26-27). Additionally, diseases associated with anion transporters have been identified. The anion transporter of SEQ ID NO: 2 therefore has a disclosed specific and substantial credible utility, as would the antibodies that selectively bind it.

Applicants conclusion that a disclosed specific and substantial credible utility is provided for the anion transporter of SEQ ID NO: 2 is additionally supported by Lohi et al. (J. Biol. Chem., Vol. 277, No. 16, pp. 14246-14254, April 19, 2002). Lohi et al. provide the amino acid sequence of SLC26A9 (Figure 1, p. 14249), among others, which is 95% identical to SEQ ID NO: 2 (see attached: "Sequence Alignment between SLC26A9 (AAK95667.1) and SEQ ID NO: 2 of the Instant Application") and is predicted to comprise 9 transmembrane helices (p. 14251, "Characteristics of SLC26A9"). The two proteins differ by only a segment of amino acids deleted in SEQ ID NO: 2. Using the transmembrane topology predicting program TMHMM (Krogh et al., J. Mol. Biol., Vol. 305, pp. 567-580, 2001), the segment where the two proteins differ in sequence is located exterior to the cell and does not affect transmembrane helix topology (see attached: "Topology of SEQ ID NO: 2 from CL000861CON Determined by TMHMM" and "Topology of SLC26A9 (AAK95667.1)

Determined by TMHMM"). The sequence variation between the two proteins occurs outside of the predicted 9 transmembrane helices. These two proteins will have the same anion transport function because the transmembrane helices responsible for anion transport in the two proteins do not differ in their amino acid sequence. Functional expression of SLC26A9 in *Xenopus* oocytes demonstrates that SLC26A9 is able to mediate at least chloride, sulfate and oxalate transport (p. 14252, Figure 4 and "Functional Analyses of SLC26A7-A9"). Other SLC26 family proteins of similar sequence to SLC26A9 also are able to transport chloride, sulfate and oxalate. Lohi et al. produce antibodies raised against a SLC26A9 peptide identical in its sequence to amino acids 720-729 of the instant SEQ ID NO: 2 (p. 14247, "Immunohistochemistry"). Using these antibodies to immunostain tissues, SLC26A9 is expressed predominantly in the lung (p. 14251, Figure 3 and p. 14253, 2nd column, 1st paragraph, last two lines), which is in agreement with the instant specification.

Members of the SLC26 family of anion exchangers have been identified with distinct human genetic diseases (Lohi et al., p. 14246, abstract and introduction). Lohi et al. identify that the regulation of ion transport and airway surface liquid is an important part of lung defense mechanisms and may contribute to different airway diseases and conclude that defects in chloride or sulfate transport function of SLC26A9 in human respiratory epithelium make it a plausible candidate for diseases of the human respiratory system (p. 14253, last paragraph). Lohi et al. characterize a SL26A9 protein that is 95% identical in amino acid sequence to the instant SEQ ID NO: 2 as an anion transporter, identify tissue and cellular location of the protein using SLC26A9 specific antibodies, and describe the functional and biological significance of the transporter and its potential role in disease.

Applicants believe that as not only the function of the instant protein has been verified, but the importance of the protein and the SLC26 family members in human disease is recognized in the art. The Lohi et al. reference has verified applicant's assertions of the functional and biological significance of the anion transporter of SEQ ID NO: 2. Therefore, a disclosed specific and substantial credible utility has been provided.

35 U.S.C. § 112

Claims 18, 20, 22, 24, 26, 28 and 30 were rejected under 35 U.S.C. § 112, 1st paragraph. The Examiner contends that as the claims are directed to antibodies against a

protein that "comprises SEQ ID NO: 2," the instant specification does not provide a written description or the guidance needed to produce an antibody which binds to any epitope other than an epitope which is contained within SEQ ID NO:2 of the instant application. This is due to the fact that epitopes are no more than 6 to 8 amino acids in length and that fusion proteins comprising a recombinant protein and an antigenic tail are well known in the art. The instant claims essentially encompass any antibody which can bind to any polypeptide or protein.

Applicants respectfully disagree. As indeed antigenic fusion-protein components are well known, antibodies against these antigens (FLAG epitope, Protein A, etc.) fused to a protein would not be encompassed by the scope of the instant claims as the claims are directed to an antibody "that selectively binds to a polypeptide, wherein the amino acid sequence of said polypeptide comprises SEQ ID NO:2..." Antibodies that bind to antigens fused to a protein of interest would not be selectively binding to a protein comprising SEQ ID NO:2. Such antibodies would bind any fusion protein comprising any protein sequence fused to those specific antigenic determinants recognized by those antibodies. As defined in the specification on page 34, lines 7-8, an antibody "selectively binds" a target peptide when it binds the target peptide and does not significantly bind to unrelated proteins. Based upon the "selectively binds" language of the claims, antibodies which are designed to bind antigens such as FLAG epitope, Protein A, etc. as part of a fusion protein would be clearly outside the scope of the claims.

35 U.S.C. § 102

Claims 18, 20, 22, 24, 26, 28 and 30 were rejected under 35 U.S.C. § 102(b) as being anticipated by Hopp et al. (US 5,011,912). The Examiner states that the claims encompass an antibody which binds to any antigenic peptide, including the FLAG epitope bound by the antibody of Hopp et al.

Applicants respectfully disagree. As Hopp et al. does not even disclose the instant polypeptide comprising SEQ ID NO: 2, the antibodies of Hopp et al. would not be able to selectively bind a protein comprising SEQ ID NO: 2. As defined in the specification on page

34, lines 7-8, an antibody "selectively binds" a target peptide when it binds the target peptide and does not significantly bind to unrelated proteins. Based upon the "selectively binds" language of the claims, antibodies which are designed to bind antigens such as those described by Hopp et al. would not be anticipatory of the instant claims.

Sequence Alignment between SLC26A9 (AAK95667.1) and SEQ ID NO: 2 of the Instant Application

The only differences between the two sequences is boldfaced.

```
BLASTP 2.2.10 [Oct-19-2004]

Reference: Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer,
Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997),
"Gapped BLAST and PSI-BLAST: a new generation of protein database search
programs",  Nucleic Acids Res. 25:3389-3402.

Query= gi|15341556|gb|AAK95667.1| putative anion transporter [Homo
sapiens]
         (791 letters)

Database: /scratch/TEMP_seq1.0.129890360477479
           1 sequences; 753 total letters

Searching.done
                                                                  Score     E
Sequences producing significant alignments:                       (bits)
Value

861CON                                                              1476
0.0

>861CON
          Length = 753

 Score = 1476 bits (3820), Expect = 0.0
 Identities = 753/791 (95%), Positives = 753/791 (95%), Gaps = 38/791 (4%)

Query: 1   MSQPRPRYVVDRAAYSLTLFDDEFEKKDRTYPVGEKLRNAFRCSSAKIKAVVFGLLPVLS 60
           MSQPRPRYVVDRAAYSLTLFDDEFEKKDRTYPVGEKLRNAFRCSSAKIKAVVFGLLPVLS
Sbjct: 1   MSQPRPRYVVDRAAYSLTLFDDEFEKKDRTYPVGEKLRNAFRCSSAKIKAVVFGLLPVLS 60

Query: 61  WLPKYKIKDYIIPDLLGGLSGGSIQVPQGMAFALLANLPAVNGLYSSFFPLLTYFFLGGV 120
           WLPKYKIKDYIIPDLLGGLSGGSIQVPQGMAFALLANLPAVNGLYSSFFPLLTYFFLGGV
Sbjct: 61  WLPKYKIKDYIIPDLLGGLSGGSIQVPQGMAFALLANLPAVNGLYSSFFPLLTYFFLGGV 120

Query: 121 HQMVPGTFAVISILVGNICLQLAPESKFQVFNNATNESYVDTAAMEAERLHVSATLACLT 180
           HQMVPGTFAVISILVGNICLQLAPESKFQVFNNATNESYVDTAAMEAERLHVSATLACLT
Sbjct: 121 HQMVPGTFAVISILVGNICLQLAPESKFQVFNNATNESYVDTAAMEAERLHVSATLACLT 180

Query: 181 AIIQMGLGFMQFGFVAIYLSESFIRGFMTAAGLQILISVLKYIFGLTIPSYTGPGSIVFT 240
           AIIQMGLGFMQFGFVAIYLSESFIRGFMTAAGLQILISVLKYIFGLTIPSYTGPGSIVFT
Sbjct: 181 AIIQMGLGFMQFGFVAIYLSESFIRGFMTAAGLQILISVLKYIFGLTIPSYTGPGSIVFT 240

Query: 241 FIDICKNLPHTNIASLIFALISGAFLVLVKELNARYMHKIRFPIPTEMIVVVVATAISGG 300
           FIDICKNLPHTNIASLIFALISGAFLVLVKELNARYMHKIRFPIPTEMIVVVVATAISGG
Sbjct: 241 FIDICKNLPHTNIASLIFALISGAFLVLVKELNARYMHKIRFPIPTEMIVVVVATAISGG 300

Query: 301 CKMPKKYHMQIVGEIQRGFPTPVSPVVSQWKDMIGTAFSLAIVSYVINLAMGRTLANKHG 360
```

```
            CKMPKKYHMQIVGEIQRGFPTPVSPVVSQWKDMIGTAFSLAIVSYVINLAMGRTLANKHG
Sbjct: 301 CKMPKKYHMQIVGEIQRGFPTPVSPVVSQWKDMIGTAFSLAIVSYVINLAMGRTLANKHG 360

Query: 361 YDVDSNQEMIALGCSNFFGSFFKIHVICCALSVTLAVDGAGGKSQVASLCVSLVVMITML 420
            YDVDSNQEMIALGCSNFFGSFFKIHVICCALSVTLAVDGAGGKSQVASLCVSLVVMITML
Sbjct: 361 YDVDSNQEMIALGCSNFFGSFFKIHVICCALSVTLAVDGAGGKSQVASLCVSLVVMITML 420

Query: 421 VLGIYLYPLPKSVLGALIAVNLKNSLKQLTDPYYLWRKSKLDCCIWVVSFLSSFFLSLPY 480
            VLGIYLYPLPKSVLGALIAVNLKNSLKQLTDPYYLWRKSKLDCCIWVVSFLSSFFLSLPY
Sbjct: 421 VLGIYLYPLPKSVLGALIAVNLKNSLKQLTDPYYLWRKSKLDCCIWVVSFLSSFFLSLPY 480

Query: 481 GVAVGVAFSVLVVVFQTQFRNGYALAQVMDTDIYVNPKTYNRAQDIQGIKIITYCSPLYF 540
            GVAVGVAFSVLVVVFQTQFRNGYALAQVMDTDIYVNPKTYNRAQDIQGIKIITYCSPLYF
Sbjct: 481 GVAVGVAFSVLVVVFQTQFRNGYALAQVMDTDIYVNPKTYNRAQDIQGIKIITYCSPLYF 540

Query: 541 ANSEIFRQKVIAKTGMDPQKVLLAKQKYLKKQEKRRMRPTQQRRSLFMKTKTVSLQELQQ 600
            ANSEIFRQKVIA                                        KTVSLQELQQ
Sbjct: 541 ANSEIFRQKVIA----------------------------------------KTVSLQELQQ 562

Query: 601 DFENAPPTDPNNNQTPANGTSVSYITFSPDSSSPAQSEPPASAEAPGEPSDMLASVPPFV 660
            DFENAPPTDPNNNQTPANGTSVSYITFSPDSSSPAQSEPPASAEAPGEPSDMLASVPPFV
Sbjct: 563 DFENAPPTDPNNNQTPANGTSVSYITFSPDSSSPAQSEPPASAEAPGEPSDMLASVPPFV 622

Query: 661 TFHTLILDMSGVSFVDLMGIKALAKLSSTYGKIGVKVFLVNIHAQVYNDISHGGVFEDGS 720
            TFHTLILDMSGVSFVDLMGIKALAKLSSTYGKIGVKVFLVNIHAQVYNDISHGGVFEDGS
Sbjct: 623 TFHTLILDMSGVSFVDLMGIKALAKLSSTYGKIGVKVFLVNIHAQVYNDISHGGVFEDGS 682

Query: 721 LECKHVFPSIHDAVLFAQANARDVTPGHNFQGAPGDAELSLYDSEEDIRSYWDLEQEMFG 780
            LECKHVFPSIHDAVLFAQANARDVTPGHNFQGAPGDAELSLYDSEEDIRSYWDLEQEMFG
Sbjct: 683 LECKHVFPSIHDAVLFAQANARDVTPGHNFQGAPGDAELSLYDSEEDIRSYWDLEQEMFG 742

Query: 781 SMFHAETLTAL 791 (SLC26A9)
            SMFHAETLTAL
Sbjct: 743 SMFHAETLTAL 753 (SEQ ID NO:2)


  Database: /scratch/TEMP_seq1.0.129890360477479
    Posted date:  Dec 2, 2005 10:16 AM
  Number of letters in database: 753
  Number of sequences in database:  1

Lambda     K      H
   0.323    0.138    0.407

Gapped
Lambda     K      H
   0.267   0.0410    0.140


Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Hits to DB: 1894
Number of Sequences: 1
Number of extensions: 55
Number of successful extensions: 2
Number of sequences better than 10.0: 1
Number of HSP's better than 10.0 without gapping: 1
```

```
Number of HSP's successfully gapped in prelim test: 0
Number of HSP's that attempted gapping in prelim test: 0
Number of HSP's gapped (non-prelim): 2
length of query: 791
length of database: 753
effective HSP length: 41
effective length of query: 750
effective length of database: 712
effective search space:   534000
effective search space used:   534000
T: 11
A: 40
X1: 16 ( 7.5 bits)
X2: 38 (14.6 bits)
X3: 64 (24.7 bits)
S1: 29 (16.4 bits)
S2: 29 (15.8 bits)
```

Topology of SEQ ID NO: 2 from CL000861CON Determined by TMHMM

Comparison of the topology of SEQ ID NO: 2 against the topology of SLC26A9 (next page) reveals that the two proteins have the same transmembrane helices and that variation in amino acid sequence occurs in the part of the protein that is outside the cell at the C-terminus (beyond residue 496).

```
# 861CON Length: 753  (amino acids)
# 861CON Number of predicted TMHs:  9   (9 Transmembrane helices predicted)
# 861CON Exp number of AAs in TMHs: 225.06861
# 861CON Exp number, first 60 AAs:  7.37263
# 861CON Total prob of N-in:        0.76188
861CON  TMHMM2.0       inside      1    97   (residues 1-97 inside cell)
861CON  TMHMM2.0       TMhelix    98   120   (Transmembrane Helix 1)
861CON  TMHMM2.0       outside   121   176
861CON  TMHMM2.0       TMhelix   177   199   (Transmembrane Helix 2)
861CON  TMHMM2.0       inside    200   205
861CON  TMHMM2.0       TMhelix   206   228   (Transmembrane Helix 3)
861CON  TMHMM2.0       outside   229   247
861CON  TMHMM2.0       TMhelix   248   269   (Transmembrane Helix 4)
861CON  TMHMM2.0       inside    270   281
861CON  TMHMM2.0       TMhelix   282   299   (Transmembrane Helix 5)
861CON  TMHMM2.0       outside   300   332
861CON  TMHMM2.0       TMhelix   333   352   (Transmembrane Helix 6)
861CON  TMHMM2.0       inside    353   372
861CON  TMHMM2.0       TMhelix   373   395   (Transmembrane Helix 7)
861CON  TMHMM2.0       outside   396   404
861CON  TMHMM2.0       TMhelix   405   427   (Transmembrane Helix 8)
861CON  TMHMM2.0       inside    428   463
861CON  TMHMM2.0       TMhelix   464   495   (Transmembrane Helix 9)
861CON  TMHMM2.0       outside   496   753   (residues 496-753 outside cell)
```

Topology of SLC26A9 (AAK95667.1) Determined by TMHMM

Comparison of the topology of SEQ ID NO: 2 (previous page) against the topology of SLC26A9 reveals that the two proteins have the same transmembrane helices and that variation in amino acid sequence occurs in the part of the protein that is outside the cell at the C-terminus (beyond residue 496).

AAK95667.1	Length: 791	**(amino acids)**			
AAK95667.1	Number of predicted TMHs:	9	**(9 Transmembrane helices predicted)**		
AAK95667.1	Exp number of AAs in TMHs:	225.50989			
AAK95667.1	Exp number, first 60 AAs:	7.46318			
AAK95667.1	Total prob of N-in:	0.75970			
AAK95667.1	TMHMM2.0	inside	1	97	**(residues 1-97 inside cell)**
AAK95667.1	TMHMM2.0	TMhelix	98	120	**(Transmembrane Helix 1)**
AAK95667.1	TMHMM2.0	outside	121	176	
AAK95667.1	TMHMM2.0	TMhelix	177	199	**(Transmembrane Helix 2)**
AAK95667.1	TMHMM2.0	inside	200	205	
AAK95667.1	TMHMM2.0	TMhelix	206	228	**(Transmembrane Helix 3)**
AAK95667.1	TMHMM2.0	outside	229	247	
AAK95667.1	TMHMM2.0	TMhelix	248	269	**(Transmembrane Helix 4)**
AAK95667.1	TMHMM2.0	inside	270	281	
AAK95667.1	TMHMM2.0	TMhelix	282	299	**(Transmembrane Helix 5)**
AAK95667.1	TMHMM2.0	outside	300	332	
AAK95667.1	TMHMM2.0	TMhelix	333	352	**(Transmembrane Helix 6)**
AAK95667.1	TMHMM2.0	inside	353	372	
AAK95667.1	TMHMM2.0	TMhelix	373	395	**(Transmembrane Helix 7)**
AAK95667.1	TMHMM2.0	outside	396	404	
AAK95667.1	TMHMM2.0	TMhelix	405	427	**(Transmembrane Helix 8)**
AAK95667.1	TMHMM2.0	inside	428	463	
AAK95667.1	TMHMM2.0	TMhelix	464	495	**(Transmembrane Helix 9)**
AAK95667.1	TMHMM2.0	outside	**496**	**791**	**(residues 496-791 outside cell)**

CONCLUSION

Claims 17-30 are pending. By way of the above amendments and arguments, Applicants have addressed all the objections and rejections raised by the Examiner. Applicants believe that the present application is now in condition for allowance.

The Examiner is invited to contact the undersigned in order to advance prosecution.

Respectfully submitted,

CELERA GENOMICS

Date: December 19, 2005

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